REMARKS

The Office Action

Claims 36, 39, and 40 stand rejected as lacking enablement. Claims 36, 39, and 40 stand rejected as obvious over Buemi et al. (Acta Derm Venereol. 82:411-417 (2002)) in view of Kim et al. (J Burn Care Rehabil. 14:541-543 (1993), Brines et al. (U.S. 2003/0104988), and Bhaskaran (US 2004/0136952). Claims 41-44 stand rejected as being obvious over Buemi in view of Dunn (Clin Podiatr Med Surg 4:413-418 (1987)), Brines, and Bhaskaran. Each of these rejections is addressed in turn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 36, 39, and 40 stand rejected as lacking enablement over the full scope of the claims. The Office states that while the specification is enabling for methods of topically applying erythropoietin (EPO) to a burn wound, it does not reasonably provide enablement for topically applying EPO to a skin graft, then applying the skin graft to the wound. According to the Office, Maggi et al. (Burns 25:237-241 (1999)) teaches that the "osmolality of the [mafenide acetate] cream causes desiccation and is cytotoxic to fresh keratinocytes, [and,] therefore, it is not useful as a topical agent for fresh autografts." The Office finds that the specification fails to enable the claimed method of treating a graft because it does not teach the osmolality of the EPO topically applied to the skin graft.

Applicant respectfully submits that Maggi is not relevant to the claimed invention. Maggi teaches that a pre-formulated anti-bacterial cream (Sulfamylon cream) caused desiccation and cytotoxicity in skin grafts. Maggi teaches that the problem identified by the Office was solved with a simple 5% aqueous solution of the same active ingredient, which was sufficient to have an anti-bacterial effect without exhibiting the desiccation and cytotoxicity of the cream formulation. The Office has not cited, and nor has the Applicant found, a reference teaching that topically applied EPO would intrinsically cause desiccation and cytotoxicity in skin grafts. Nor has the Office has provided any rationale for why one skilled in the art would expect an antibacterial topical formulation to have had similar properties to a topical formulation containing a biological ingredient like EPO protein. Maggi does not stand for the proposition

that skin grafts cannot be pre-treated with a topical formulation prior to application to a wound. Rather, Maggi simply teaches that one particular formulation of a drug other than EPO was not compatible with this approach, while other formulations were compatible. Therefore, the teachings of Maggi are not evidence that the preparation of topical formulations of EPO is a particularly unpredictable field of scientific endeavor. The amount of experimentation necessary to determine the optimal dosage and administration schedule of applying EPO to a graft prior to engraftment would have required only routine experimentation. Consequently, the specification would have enabled one skilled in the art to perform the claimed invention over the full scope of the claims without undue experimentation and, therefore, the rejection for lack of enablement should be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 36, 39, and 40

Claims 36, 39, and 40 stand rejected under 35. U.S.C. § 103(a) for obviousness over Buemi in view of Kim, Brines, and Bhaskaran. Buemi is cited as teaching administration of EPO in a cutaneous flap animal model, resulting in improved wound healing. The Office asserts that Buemi teaches topical administration of EPO, but concedes that Buemi does not teach administration of EPO to treat burn wounds. Kim is cited as teaching subcutaneous administration of EPO to a burn victim. Brines and Bhaskaran are cited as teaching EPO glycosylation variants and conjugation with PEG, respectively.

The Office concludes that "Buemi et al. teach that rHuEPO administration can improve the wound-healing process in both early and late stages of injury. Kim et al. teach that EPO is used to prevent blood loss in burn patients. It would be obvious to also apply EPO to burn wounds because EPO is used to prevent blood loss in burn patients."

Applicant respectfully submits that the Office errs in its interpretations of Buemi and Kim. Contrary to the Office's assertion, both Buemi and Kim teach subcutaneous administration of EPO rather than topical administration, as claimed. Buemi teaches a systemic dosage of EPO by administering an amount proportional to the total body weight of the treated rat (e.g., "a subcutaneous administration of 300IU/kg/day of rHuEpo." (Buemi, pg. 412, 1st paragraph)).

The 4000 U Epogen-Epoetin ALFA taught by Kim is a standard systemic dosage of EPO. Therefore, neither reference teaches or suggests the topical application of EPO to treat a burn wound in general or the topical application to a graft prior to engraftment in particular.

The Office states that "Kim et al. teach that EPO is used to prevent blood loss in burn patients." However, Kim merely reports a case study whereby a burn victim treated with skin graft procedures refused blood transfusions for religious reasons (see page 241, third paragraph).. EPO was administered subcutaneously, presumably in order to induce red blood cell production to compensate for the unavailability of a blood transfusion. This intent can be inferred from the statement that "patient's hemoglobin and hematocrit remained stable at 7 gm/dl and 2%, respectively, [during the period of EPO treatment]." (Page 542, 1st paragraph).

One skilled in the art at the time of the invention would not have been motivated to modify the method of repeated subcutaneous administration to preserve hemoglobin and hematocrit levels as taught by Kim to a method of topical administration of EPO to a burn wound or graft prior to engraftment, as currently claimed. The Office has not cited any reference which teaches that topical administration of EPO to a wound or a skin graft (as currently claimed) would result in stabilization of a patient's hemoglobin and hematocrit levels. Consequently, the modification to Kim proposed by the Office would render the method of Kim unsatisfactory for its intended purpose (maintenance of hemoglobin and hematocrit levels). According to M.P.E.P. § 2143.01(V), "a proposed modification [to a prior art method] cannot render the prior art unsatisfactory for its intended purpose" because "there is no suggestion or motivation to make the proposed modification" (citations omitted). Therefore, when taken together, Buemi and Kim do not teach or suggest a method of treating a burn by topically administering EPO to a graft prior to engraftment. Furthermore, the teachings of Brines and Bhaskaran do not remedy this deficiency. The rejection of claims 36, 39, and 40 for obviousness should be withdrawn.

Claims 41-44

The Office rejects claims 41-44 as being obvious over Buemi in view of Dunn (Clin Podiatr Med Surg 4:413-418 (1987)), Brines, and Bhaskaran. The teachings of Buemi, Brines, and Bhaskaran are discussed above. The Office cites Dunn as teaching "the use of mechanical

debridement in dermal wounds to remove necrotic and devitalized tissue" and teaching "that the process helps with effective wound healing and decreases the risk of infection." As previously stated, Buemi does not teach topical administration of EPO and, consequently, does not teach administration of EPO into blood coagulum. As this limitation is not taught by any of the cited references, this rejection could be withdrawn on this basis alone.

Furthermore, Dunn teaches that "vigorous, repeated debridement" is "essential" and is to be followed by "high pressure irrigation and frequent wet to dry fine mesh gauze dressings" (abstract).

The Office must articulate a clear, explicit rationale to support a conclusion that a claim is obvious. M.P.E.P. 2141(III) states:

> The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting *In re Kahn,* 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" (Citations omitted).

The Office fails to provide any rationale for how the method of Dunn is compatible with the claimed method of administering EPO to blood coagulum following debridement. The brief description of Dunn cited by the Office appears to teach cleaning and repetition of irrigation and drying in order to minimize blood coagulum prior to wound dressing. Because neither Buemi nor Dunn teach or suggest the administration of EPO to blood coagulum, and because one skilled in the art would not have been motivated to combine the teachings of Dunn with the administration of EPO to the blood coagulum, the rejection of claims 41-44 for obviousness should be withdrawn.

Conclusion

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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